



Case Report:

Perianal Ulcer and Diabetes Insipidus: A Rare Presentation of Langerhans Cell Histiocytosis in an Adult Male

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Citation

Beng NC, Kosai NR, Yee LS, Das S, Subasri A, Rajan R. Perianal Ulcer and Diabetes Insipidus: A Rare Presentation of Langerhans Cell Histiocytosis in an Adult Male. *Online J Health Allied Scs.* 2017;16(2):13. Available at URL:<http://www.ojhas.org/issue62/2017-2-13.html>

Submitted: May 7, 2017; Accepted: July 18, 2017; Published: July 30, 2017

Abstract: Langerhans cell histiocytosis (LCH), previously known as Histiocystosis X, is a rare idiopathic disease caused by a build-up of langerhan cells in the body. LCH has a heterogenous form of clinical presentation and presents with varying degree of severity. The severity often depends on the disease burden. LCH can manifest as a unifocal disease, multifocal-unisystem or multifocal-multisystem disease with the latter being more fatal than the rest. Risk organ involvement confers a grim prognosis. Perianal lesions are extremely rare skin manifestation of LCH with only few cases reported in the past. Vinca-alkaloids and steroid therapy have been shown to be effective in a large percentage of those presenting with LCH. This case report highlights the diagnosis and management of LCH presenting as a painful perianal ulcer in the background of newly diagnosed diabetes insipidus.

Key Words: Ulcer, Histopathology, Anus, Endocrine, Langerhans cell, Pituitary, Skull, Diabetes insipidus

Introduction:

Langerhans cell histiocytosis (LCH) is a rare disease. Idiopathic in nature, it is estimated to affect one to five children and one to two adults per 1 million population. Approximately 1200 new cases per year are reported in the United States of America alone. Seen more in male Caucasians, LCH affects individuals from all groups ranging from neonate to elderly population.(1-3) It affects almost every organ in the body from skin to lung, hepatobiliary, bone, salivary gland and even the central nervous system. The severity often depends on the disease burden. LCH can manifest as a unifocal disease, multifocal-unisystem or multifocal-multisystem disease with the latter being more fatal

than the rest.(4) Our report highlights an interesting manifestation of LCH in an adult who presented with complaint of perianal ulcer in the background of newly diagnosed diabetes insipidus.

Case Report

A 52-year-old male, known to be Hepatitis B positive presented to the emergency department with complaint of painful swelling over the perianal region for the past 2 years which had shown insidious growth. The swelling was associated with minimal sero-purulent discharge. There was no history of fever, nausea or vomiting. He was able to tolerate orally and had no alteration in bowel habit or similar swelling elsewhere. Examination of the perianal region revealed a foul-smelling, inflamed perianal ulceration measuring about 15 x 8 cm extending to the sacral region and the anorectal junction. The anal tone was lax possibly secondary to sphincter involvement. Examination of all other systems were unremarkable. Patient was admitted for full workup and further investigation. Colonoscopy was performed with no other synchronous or skip lesion seen throughout the length of the large bowel. Intubation of the terminal ileum was also negative for any ulceration or mass.

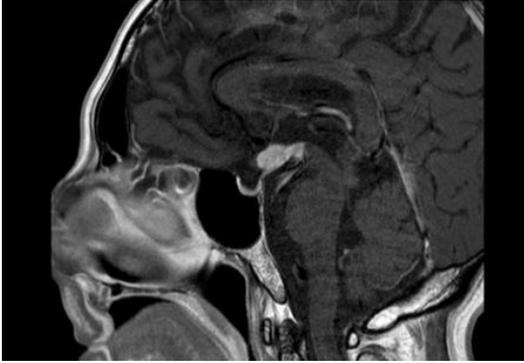


Fig.1: Midline sagittal T1-weighted MR image shows thickening of the pituitary stalk.

His blood investigation revealed hypernatremia and hypothyroidism. His daily urine output measured approximately 4 liters per day. He was diagnosed to have pan hypopituitarism by the endocrinologist and was started on desmopressin and hydrocortisone. Magnetic resonance imaging of the brain revealed an avidly enhancing extra axial lesion consistent with pituitary involvement of LCH (Fig.1). Fluid resuscitation and correction of electrolyte anomalies were undertaken. A diverting colostomy was performed two days later to facilitate wound dressing of the anorectal lesion. Wedge biopsy of the anorectal lesion was also taken in the same setting.

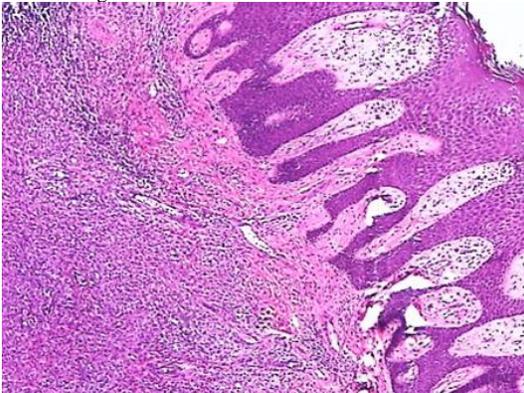


Fig.2: Magnified electron microscopic image showing sheets of atypical Langerhans cells from the reticular dermis is seen infiltrating the oedematous papillary dermis and focally ulcerating the epidermis.

Histopathology examination of the biopsy specimen revealed epidermal ulceration with underlying dermal edema and granulation tissue formation with extensive abscess. Atypical cells were also noted presenting as nodular sheets in the reticular dermis as well as in the form of clusters invading the edematous papillary dermis and acanthotic epidermis (Fig.2). The atypical cells were characterized by abundant amphophilic cytoplasm with large vesicular nuclei with nuclear grooves. There were no prominent nucleoli observed (Fig.3). The clusters were accompanied by lymphocytes, perivascular eosinophils and neutrophils (Fig.4). Immunohistochemistry studies of the same sample tested positive for CD1a, S100, CD10, Vimentin, CD45, p53, and occasionally for CD 117 (Fig.5).

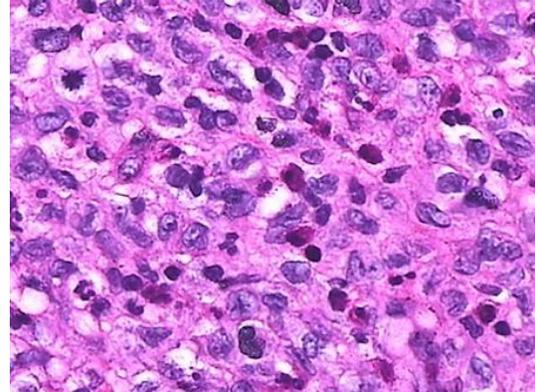


Fig.3: Magnified electron microscopic image showing characteristic features of the atypical Langerhans cells such as abundant eosinophilic cytoplasm with large nuclei and intranuclear grooves in the absence of nucleoli.

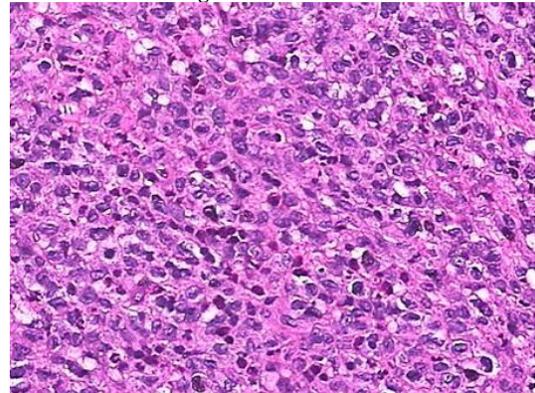


Fig.4: Magnified electron microscopic image showing eosinophils, neutrophils and lymphocytes accompanying the atypical Langerhan Cells.

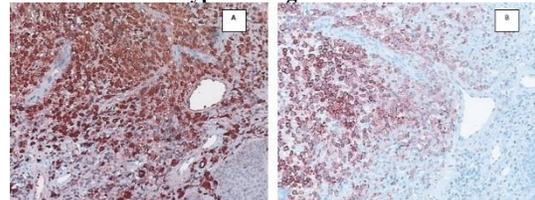


Fig.5: Immunohistochemical study of the biopsy specimen tested positive for S100(A) and CD1a(B).

A full body CT scan was performed leading to a final diagnosis of Langerhans cell histiocytosis with multisystem disease (central nervous system and skin). He was then referred promptly to the hematology team who then started him on a 6-week course of Vinblastine and Prednisone. At the time of preparing this manuscript, our patient unfortunately had defaulted treatment following completion of the initial therapy.

Discussion

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by overproduction and accumulation of a specific type of white blood cell called histiocyte in the various tissues and organs of the body. LCH results from the clonal proliferation of immunophenotypically and functionally immature, morphologically rounded LCH cells along with lymphocytes, macrophages, eosinophils and occasionally, multinucleated giant cells.(1) LCH usually presents as a childhood disease. Prevalence is higher among children compared to adults, with only 1 in every 1 million adults affected by the disease.(2,3) Clinically, LCH can present as a

unifocal or multifocal disease confined to just one or affecting many systems at the same time. In a report based on a German registry with 121 confirmed cases of LCH, 62% had single-organ involvement while remaining 38% showed multisystem involvement. The median age at diagnosis within that cohort was 44 years \pm 12.8 years, with the most common organ involved being the lung followed by bone and skin.(4)

There have been numerous reports on skin involvement in LCH. They commonly involve intertriginous and seborrheic areas of the skin such as the posterior aspect of the pinna, scalp and axilla. LCH in such areas often appear pruritic mimicking seborrheic dermatitis. Perianal involvement is an extremely rare presentation of LCH, with a limited number of cases reported in literature.(5-8) There are also equally limited number of reports pertaining to the presence of central diabetes insipidus as an early manifestation of LCH.(9) Patients who present with isolated diabetes insipidus should be carefully observed for onset of other symptoms or signs characteristic of LCH. At least 80% of patients with diabetes insipidus have been shown to also involve other organ systems such as bone (68%), skin (57%), lung (39%), and lymph nodes (18%).(10) Multisystem disease with risk organ involvement such as liver, spleen, bone marrow and lung has been associated with poorer prognosis by the International LCH Study of the Histiocyte Society.(11)

The diagnosis of LCH is based on morphologic identification of the LCH cells and immunophenotypic examination of the biopsy specimen from the affected site. Positive stain with CD1a and/or Langerin (CD207) is required for definitive diagnosis.(12,13) Ultrastructural demonstration of cytoplasmic Birbeck granules is not necessary in the presence of a positive Langerin stain.(14)

The lack of clinical trials limits the ability to make evidence-based recommendations for treatment of LCH in adults. Generally, focal bone lesions may be curetted while skin lesions excised or treated with topical medications. Multisystem disease would require administration of vinca alkaloids with or without corticosteroids. A 6 week course of vinblastine and prednisone has been proven effective with minimal side effects.(15) Patients without risk organ involvement have excellent long term survival prognosis if they respond to the initial 6 week therapy. The treatment is then followed up with a one year course of mercaptopurine, vinblastine and prednisone.(16) Patients with risk organ involvement and those who do not show improvement with the initial therapy, have an unfavourable prognosis.(17,18) Had our patient not defaulted, the management plan for him was to continue with the one year therapy post completion of the initial 6 week course. The decision was made in lieu of risk organ involvement despite demonstrating multisystem involvement.

Conclusion

Although perianal region is not a typical site of presentation of LCH disease, this disorder should be considered when seen alongside an unlikely endocrine disorder such as diabetes insipidus. Biopsy and immune-histochemical analysis of the lesion is key to diagnosing this entity. Radiological imaging of the body will help decide on extent of involvement and subsequently prognosticate the outcome. Early treatment with vinblastine and prednisone followed by a one year course of mercaptopurine, vinblastine and prednisone have been proven beneficial in LCH except for the multifocal-multisystem group with risk organ involvement.

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